

amyloid form of PAP₂₄₈₋₂₈₆ had little effect on either vesicle aggregation or fusion. To further investigate this effect we have solved the structure of PAP₂₄₈₋₂₈₆ in SDS micelles. A largely α -helical conformation of PAP₂₄₈₋₂₈₆, lying parallel to the membrane surface, is implicated in promoting bridging interactions between membranes by the screening of the electrostatic repulsion that occurs when two membranes are brought into close contact. This suggests non-specific binding of small oligomeric forms of SEVI in an α -helical conformation to lipid membranes may be an additional mechanism by which SEVI enhances the infectivity of the HIV virus.

Lipids and Signaling on Membrane Surface

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The Preferential Reconstitution Of Ampa Receptor Proteins Into Model Lipid Domains With Cholesterol Studied By Atomic Force Microscopy - an Imaging And Force Spectroscopy Study

Chandra Ramanujan¹, Nahoko Kasai², Matthew Suggit¹, Jelena Baranovic¹, Keichi Torimitsu², John F. Ryan¹.

¹University of Oxford, Oxford, United Kingdom, ²NTT-BRL, Atsugi, Japan.

In our research we have conducted an atomic force microscopy (AFM) study of trafficking-like behaviour of neural receptor proteins into lipid raft-like domains. In our initial research we formed artificial rafts by varying a mixture of four phospholipids found in the synapse in order to mimic a synaptic membrane. The most commonly occurring receptor protein in the central nervous system, the AMPA receptor (α -amino-3-hydroxy-5-methyl-4-isoxazole propionic acid), was then reconstituted into these mixtures. The results show a preferential reconstitution of these membrane proteins into lipid rafts of a certain height. AMPA receptors are implicated in long term potentiation, a process thought to underlie learning and memory, with up-regulation of AMPAR numbers in the post-synaptic membrane possibly being a key component of this process.

In order to come closer to the mixtures naturally occurring in the synapse we furthered these studies to incorporate cholesterol. The results were a preferential reconstitution of AMPAR proteins but this time into the low domain when cholesterol is present. These surprising results were better understood when we treated this system as a ternary mixture with gel phase lipids, liquid phase lipids and cholesterol acting as an impurity. We studied the phases in terms of the domain heights as well as their mechanical properties. When cholesterol was present, the protein-deficient high domains were stiffer and more viscous.

The lateral extent of the lipid domains is typically ~100nm, so they have structural similarities with the lipid rafts observed to occur in synaptic membranes, albeit with much simpler composition. Dynamic AFM measurements reveal information about the mobility of receptors within and between domains which may shed light on this process.

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Piezoelectricity of phospholipids: Are cell membranes also piezoelectric? Antal Jakli.

Kent State University, Kent, OH, USA.

Recently it was found¹ that mechanical deformation of films of L- α -phosphatidylcholine in the L_a phase induces an electric polarization. It was suggested that this effect is due to the chiral smectic A (SmA*) type liquid crystal structure of the bilayers, which under molecular tilt becomes a ferroelectric (SmC*) phase, where the electric polarization is normal to the tilt plane. However no control measurement on the racemic material has been presented to prove this suggestion. Here we demonstrate that indeed the chirality of phospholipids makes fluid lipid bilayers piezoelectric. By periodically shearing and compressing nonaqueous lamellar phases of synthetic right enantiomer 2,3-Dihexadecanoyl-sn-glycero-1-phosphocholine (D-DPPC) the synthetic left enantiomer 1,2-Dihexadecanoyl-sn-glycero-3-phosphocholine (L-DPPC) lipids and their racemic mixture (DL-DPPC), we induced a tilt of the molecules with respect to the bilayer normal and produced electric current perpendicular to the tilt plane, with the chiral lipids only. Because most of the living cell membranes contain chiral lipids, we hypothesize that piezoelectricity may have a role in the function of cell membranes. For example, this coupling allows for a wide variety of sensory possibilities of cell membranes such as mechano-reception, magneto-sensitivity, and proton membrane transport. Preliminary results on electromechanical couplings in *Saccharomyces cerevisiae* (Baker's yeast) and their protoplasts will be also reported and discussed.

Endnotes

¹A. Jakli, J. Harden, C. Notz and C. Bailey, *Liquid Crystals*, 35 (4), 395-400 (2008).

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Gastrin-Releasing Peptide Adopts An Orientation Parallel To The Membrane Plane As A Preferred Orientation In DMPC Bilayers: Multiple Molecular Dynamics Simulations

Priyanka Prakash Srivastava.

Indian Institute of Technology, Kanpur, Kanpur, India.

Gastrin-releasing peptide (GRP) binds to GRP-receptor (GRPR), a member of GPCR family. GRP is one of the bombesin peptides and they are implicated in obesity and cancer. Understanding the mechanism of GRP-GRPR interactions at molecular level is extremely significant and requires the knowledge of the structure of peptide-receptor complex. Since the complex structure is not available, the structures of ligand and the free receptor could be used to model the complex. GRP is flexible in aqueous medium but it is likely to adopt a stable structure when it binds to membrane according to "Membrane Compartments Theory" [*Biopolymers* 37, 5-16 (1995)].

The C-terminal decapeptide of GRP is biologically active and is modeled as a helix using a related peptide structure determined in SDS micelles [*FEBS Lett.* 460, 263-269 (1999)]. Its amino acid sequence is GNHWAVGHLM. We carried out multiple independent simulations of GRP peptide in explicit DMPC bilayers which differed in the orientation of GRP inside the bilayers and force-field. At the end of 10 to 20 ns production runs, five out of six simulations resulted in the peptide orientation that is nearly parallel to the membrane plane. This indicates that this orientation is a preferred one and is independent of CHARMM or GROMOS force-fields. In the sixth simulation, the peptide was deeply inserted inside the bilayer. We analyzed the stability of helix, interaction of individual residues with different lipid components and water penetration in both layers. The helix structure is stable in majority of the simulations. Our results indicate that the residues Gly-7 and His-8 are important in maintaining the helical structure and orienting the peptide.

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Lipid Composition Modulates the Stability of DNA Acting as Model Membrane-bound Receptors

Paul A. Beales, T. Kyle Vanderlick.

Yale University, New Haven, CT, USA.

Many important signaling processes occur in the interactions between lipid organelles: a multitude of ligands and receptors are localized to the surface of lipid structures and vary in many ways, including their length and the strength of their interactions. DNA strands with hydrophobic modifications anchor to the surface of lipid membranes. These membrane-anchored DNA diffuse within the lipid matrix and can bind specifically to their complement: minimal properties of real membrane receptors. The properties of these DNA "receptors" can be varied systematically to explore the physical advantages of variables such as receptor length, binding strength and repeated sequences in the binding domain.

We show that the binding equilibrium between DNA-functionalized vesicles is dependent upon lipid composition. We develop a model as a framework to understand this phenomenon by extension of the Bell model to the non-constant force-fields between lipid membranes. We find that the inter-membrane interactions can either suppress or favor receptor binding and discuss the possible implications for biological receptor-mediated signaling processes.

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Phosphatidylinositol-(4,5)-bisphosphate Acting As A Ligand Of PKC α Modulates The Membrane Localization Of This Enzyme In Living Cells

Juan C. Gómez-Fernández, Consuelo Marin-Vicente, Francisco E. Nicolas, Senena Corbalán-García.

Univesidad de Murcia, Murcia, Spain.

Rapamycin-triggered heterodimerization strategy is becoming an excellent tool for rapidly modifying phosphatidylinositol(4,5)-bisphosphate [PtdIns(4,5)P₂] levels at the plasma membrane and for studying their influence indifferent processes. In this work, we studied the effect of modulation of the PtdIns(4,5)P₂ concentration on protein kinase C (PKC) α membrane localization in intact living cells. We showed that an increase in the PtdIns(4,5)P₂ concentration enlarges the permanence of PKC α in the plasma membrane when PC12 cells are stimulated with ATP, independently of the diacylglycerol generated. The depletion of this phosphoinositide decreases both the percentage of protein able to translocate to the plasma membrane and its permanence there. Our results demonstrate that the polybasic cluster located in the C2 domain of PKC α is responsible for this phosphoinositide-protein interaction. Furthermore, the C2 domain acts as a dominant interfering module in the neural differentiation process of PC12 cells, a fact that was also supported by the inhibitory effect